IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

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01/08/2007 /Pamela Gerik/
Date Pamela Gerik

SUPPLEMENTAL APPEAL BRIEF

Sir/Madam:

A Notice of Appeal and Request for Pre-Appeal Brief Review was filed August 29, 2005. The Notice of Panel Decision from Pre-Appeal Brief Review was mailed October 28, 2005. The original Appeal Brief was filed November 28, 2005. This Supplemental Appeal Brief is submitted in response to a Notice of Non-Compliant Brief mailed December 11, 2006. The brief was cited as non-compliant for failing to contain the proper explanation of the subject matter as defined in each of the independent claims involved in the appeal and, specifically, independent claim 39. The Notice of Appeal and Request for Pre-Appeal Brief Review were filed following mailing of a final Office Action on June 29, 2005. Appellant hereby appeals to the Board of Patent Appeals and Interferences from the final rejection of claims 1-7, 40, and 41, and respectfully requests that this appeal be considered by the Board.

I. REAL PARTY IN INTEREST

The subject application is owned by Luminex Corporation, a corporation having a place of business at 12212 Technology Boulevard, Austin, Texas 78727-6115.

II. RELATED APPEALS AND INTERFERENCES

No other prior and pending appeals, interferences, or judicial proceedings are known to Appellant or Assignee which would directly affect or be directly affected by or have a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

Claims 1-7 and 39-41 are pending. Claims 1-7, 40, and 41 stand finally rejected. Claim 39 is withdrawn at this time. Claims 8-38 were canceled. Claims 1-7, 40, and 41 are being appealed.

IV. STATUS OF AMENDMENTS

No amendments to the claims have been filed subsequent to their final rejection. The Claims Appendix attached hereto reflects the current state of the claims.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Appellant's claimed subject matter as recited in claim 1 includes a Multi-Analyte Profile (MAP) Test Panel that includes 75 or more subsets of microspheres (Specification -- page 3, lines 27-28). The microspheres of one subset are distinguishable from those of another subset by their characteristic fluorescence signatures (Specification -- page 3, line 29-30). The microspheres of the one subset are coupled to at least one reagent designed to interact selectively with a predetermined analyte (Specification -- page 3, lines 25-27).

Appellant's claimed subject matter as recited in claim 7 also includes a kit for assaying 75 or more predetermined analytes in a single pass through a flow analyzer comprising a Multi-Analyte Profile (MAP) Test Panel that includes 75 or more subsets of microspheres (Specification -- page 3, lines 27-28; page 4, lines 8-10). The microspheres of one subset are

distinguishable from those of another subset by their characteristic fluorescence signatures (Specification -- page 3, line 29-30; page 4, lines 10-11; page 14, lines 18-20; page 20, lines 26-29). The microspheres of the one subset are coupled to at least one reagent designed to interact selectively with a predetermined analyte (Specification -- page 3, lines 25-27; page 4, lines 10-12; page 14, lines 20-21; page 20, lines 24-25). The kit also includes vials, supplemental reagents, or any combination thereof (Specification -- page 21, lines 1-2).

Appellant's claimed subject matter as recited in claim 39 also includes a method of using a Multi-Analyte Profile (MAP) Test Panel to assess a subject's health or medical condition. For example, the claimed method may include (a) exposing the one or more test samples obtained from a subject to a Multi-Analyte Profile (MAP) Test Panel comprising 20 or more subsets of microspheres (Specification -- page 4, lines 13-17). As noted above, the microspheres of one subset may be distinguishable from those of another subset by their characteristic fluorescence signatures (Specification -- page 4, lines 17-18; page 14, lines 17-21). The microspheres of one subset also harbor at least one reagent designed to interact selectively, if not specifically, with a predetermined analyte, which interaction generates biochemical data concerning the predetermined analyte (Specification -- page 4, lines 18-20).

The claimed method may also include (b) gathering the biochemical data, if any, generated from the exposure (Specification -- page 4, lines 20-21). The claimed method may also include (c) comparing the biochemical data generated from the one or more samples obtained from the subject with accumulated biochemical data generated from test samples taken periodically from at least about 1,000 individuals over a given time interval, which accumulated biochemical data provide a relationship between one or more predetermined analytes and the health or medical condition of a plurality of individuals whose accumulated biochemical data share similar features (Specification -- page 4, lines 21-26). The claimed method may also include (d) assessing the health or medical condition of the subject based, at least in part, on the results of the comparison (Specification -- page 4, lines 26-27).

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Claims 1-7, 40, and 41 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2. Claims 1-7, 40, and 41 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kettman et al. (Cytometry (1998) 33:234-243) (hereinafter "Kettman") in view of Ekins (Journal of Pharmaceutical and Biomedical Analysis (1989) 7: 155-168) (hereinafter "Ekins").

VII. ARGUMENT

The contentions of Appellant with respect to each ground of rejection presented for review, and the basis therefore, with citations of the statutes, regulations, authorities, and parts of the record relied on are presented herein for consideration by the Board.

Rejection under 35 U.S.C. § 112, second paragraph

Claims 1-7, 40, and 41

1. The term "interact selectively" does not render the claims indefinite.

Claim 1 recites in part: "wherein the microspheres of the one subset are coupled to at least one reagent designed to interact selectively with a predetermined analyte." Claim 7 also recites this limitation.

The term "interact selectively" recited in the claims is definite when analyzed in light of the content of the particular application disclosure, the teachings of the prior art, and the claim interpretation that would be given to the term by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. For example, the term "interact selectively" is described in the Specification on page 4, lines 1-3, page 15, lines 11-17, and page 20, line 24 to

page 21, line 2. When analyzed in light of the content of the present application disclosure, the term "interact selectively" sets out and circumscribes the presently claimed subject matter with a reasonable degree of clarity and particularity. In addition, the term "interact selectively" is known in the art as evidenced by the teachings of the prior art. For example, a search of the database of patents issued from 1976 to present that is available on the USPTO website indicates a number of patents that include the term "interact selectively." Examples of patents that particularly illustrate that the term "interact selectively" was known by one possessing the ordinary level of skill in the pertinent art about the time the invention was made include U.S. Patent Nos. 6,406,913 to Ullman et al., 6,537,749 to Kuimelis et al., and 6,689,887 to Kerwin et al.

Accordingly, based on the content of the disclosure of the present application and the teachings of the prior art, one possessing the ordinary level of skill in the pertinent art at the time the invention was made would interpret the claims, and particularly the term "interact selectively" as recited in the claims, as clearly and particularly setting out and circumscribing a particular subject matter. The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity. Definiteness of claim language must be analyzed, not in a vacuum, but in light of: (A) The content of the particular application disclosure; (B) The teachings of the prior art; and (C) The claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. MPEP 2173.02.

Furthermore, the term "interact selectively" is not assigned any special meaning in the specification. Therefore, even if the term "interact selectively" can have a number of meanings according to the teachings of the prior art, since the term is not assigned a special meaning in the specification, the term "interact selectively" can have any of these meanings. A fundamental principle contained in 35 U.S.C. 112, second paragraph is that applicants are their own lexicographers. They can define in the claims what they regard as their invention essentially in whatever terms they choose so long as any special meaning assigned to a term is clearly set forth in the specification. MPEP 2173.01.

2. A claim cannot be rejected as indefinite simply because it is broad in scope.

The final Office Action mailed June 29, 2005 (hereinafter "the Final Office Action") states:

> Claims 1 and 7 continue to recite "one reagent designed to interact selectively with a pre-determined analyte." It remains unclear what the metes and bounds of "selectively" are in the claim. Applicant has pointed to several pieces of prior art to support the argument that "the term 'interact selectively' is known in the art". Furthermore, Applicant states that "the term is not assigned any special meaning in the specification". It is evident that from the various pieces of prior art that "selectively" can mean a number of things. Without clarification of the metes and bounds intended by Applicant, the term remains indefinite and the rejection is maintained (Final Office Action -- pages 2-3).

The Examiner, therefore, appears to be equating breadth of a claim term with indefiniteness. However, even if a claim term such as "interact selectively" is broadly defined in the teachings of the prior art, breadth of claim terminology does not render the claim indefinite. A claim cannot be rejected as indefinite simply because it is broad in scope. Breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597 (CCPA 1971). MPEP 2173.04.

3. The scope of the subject matter embraced by claims 1 and 7 is clear, and Applicants have not otherwise indicated that they intend the invention recited in claims 1 and 7 to be of a scope different from that defined in the claims.

Since the scope of the subject matter embraced by claims 1 and 7 is clear for at least the reasons set forth above, and since Applicants have not otherwise indicated that they intend the invention recited in claims 1 and 7 to be of a scope different from that defined in the claims, claims 1 and 7 comply with 35 U.S.C. 112, second paragraph. If the scope of the subject matter embraced by the claims is clear, and if applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. 112, second paragraph. MPEP 2173.04. As such, the term "interact selectively" does not render claims 1 and 7 indefinite.

4. The basis for the § 112, second paragraph, rejection of claims 1 and 7 is improper.

The second paragraph of 35 U.S.C. 112 is directed to requirements for the claims: The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention. MPEP 2171. For at least the reasons set forth above, the claims particularly point out and distinctly define the metes and bounds of the subject matter which Applicants regard as their invention. As such, claims 1 and 7 meet the requirements under 35 U.S.C. § 112, second paragraph.

* * *

As explained in the above arguments, claims 1 and 7 particularly point out and distinctly claim the subject matter which Applicants regard as the invention. For at least these reasons, claims 1 and 7, as well as dependent claims 2-6, 40, and 41, are definite. Therefore, the rejection of claims 1-7, 40, and 41 under 35 U.S.C. § 112, second paragraph is asserted to be erroneous.

Rejection under 35 U.S.C. § 103(a) over Kettman in view of Ekins

A. Claims 1-2, 5-7, 40, and 41

1. The cited art does not teach, suggest, or provide motivation for a Multi-Analyte Profile (MAP) Test Panel that includes 75 or more subsets of microspheres.

Independent claim 1 recites in part: "[a] Multi-Analyte Profile (MAP) Test Panel comprising 75 or more subsets of microspheres." Independent claim 7 recites a similar limitation.

There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to combine Kettman and Ekins as suggested in the Final Office Action. For instance, Kettman discloses an assay that is performed using up to 64 multiplexed microsphere sets. In particular, Kettman states that "In the

parameters used for designing microspheres to be used for multiplexing, uniformity (low CV) is an important issue. The more uniform the population, the more sets that can be blended and used in the same mixture." (Kettman -- page 239). Therefore, Kettman discloses that the number of microsphere sets that can be used in a multiplexed array is limited by the uniformity of the microspheres. In addition, Kettman states that "The median MFI of the population (Fl 2 and Fl 3) should be placed as close to the center of the classification criteria as possible. Microspheres from one set do not fall into the classification criteria for a neighboring set of microspheres. This feature is related to the uniformity of the fluorescence among the members of each microsphere set, that is, the CV." (Kettman -- page 239). Therefore, Kettman teaches that the number of microsphere sets that can be used in a multiplexed array is limited by the fluorescence uniformity among the microsphere members of each set.

Kettman also discloses how fluorescence is imparted to the microspheres. For instance, Kettman states that "Several observations have been made regarding the use of dyes dissolved in the microspheres. Because the dyes are inside the microspheres, solvent conditions will not affect the dye characteristics." (Kettman -- page 241). Therefore, Kettman teaches that the fluorescence used to determine the set to which a microsphere belongs is generated by excitation of dyes located inside the microspheres. In addition, Kettman states that "Although the microsphere population is reasonably uniform, small differences in size and or composition alter the relative dyeing efficiency. Additionally, as the dye content is increased, the spectrum of the combination of two dyes changes." (Kettman -- page 241). Therefore, Kettman teaches that variations in the microspheres themselves and the dye content within the microspheres affect the fluorescence used to determine the set to which a microsphere belongs. Consequently, Kettman teaches that the number of microsphere sets that can be included in an assay is limited at least in part by the variations in the microspheres themselves and the dye content within the microspheres. The limitations in the number of microsphere sets that can be used in an assay disclosed by Kettman is perhaps why Kettman states that "This measurement system can analyze up to 64 analytes in a single sample" (Kettman -- abstract, emphasis added) using 64 multiplexed microsphere sets (Kettman -- title, emphasis added).

In contrast, Ekins discloses a multi-analyte immunoassay that utilizes antibody molecules attached to a solid support. In particular, Ekins states that "exposure of a small number of antibody molecules (in the form, for example, of a 'microspot' located on a solid support) to an analyte-containing fluid results in an antibody binding site occupancy which reflects the analyte concentration in the medium." (Ekins -- page 166). Ekins also states that "This can be conveniently achieved by labeling each of the antibodies used with different markers; for example, a pair of radioactive, enzyme or chemiluminescent markers." (Ekins -- page 166). Therefore, Ekins teaches that the labels that are used to distinguish one antibody from another are coupled to the antibodies themselves.

Consequently, unlike the assay of Kettman in which the fluorescent markers are dissolved within the solid substrate (e.g., microspheres), the markers used by Ekins are not dissolved or otherwise integrated into a solid substrate. In particular, as shown in Figure 6 of Ekins, the fluorescent label that emits the ß fluorophore is attached to antibodies, and the antibodies are attached to the solid substrate. Therefore, the fluorescent markers of Ekins are external to the solid substrate. In addition, Ekins states that "The concept is also being exploited in the development of 'multi-analyte' immunoassay systems, enabling the simultaneous measurement of tens or even hundreds of substances simultaneously in the same small sample." (Ekins, Abstract, page 155). Therefore, unlike the assays of Kettman, which as taught by Kettman are limited at least in part by the variations in the microspheres themselves and the dye content within the microspheres, Ekins appears to teach that using fluorescently labeled antibodies located externally to a solid substrate in an assay does not limit the assay to measuring up to 64 analytes in one sample.

Kettman and Ekins, therefore, rely on completely different technologies to create an assay. In particular, Kettman and Ekins teach using dramatically different technologies for fluorescently-labeling the probes of the assays. In addition, as is known by one possessing the ordinary level of skill in the art at the time the invention was made, the technology for coupling fluorescent labels to antibodies cannot be used to incorporate fluorescent labels into a microsphere. Therefore, there is no suggestion or motivation to combine the teachings of Ekins with the teachings of Kettman to attempt to increase the number of microsphere sets that can be

used in the assays of Kettman. Consequently, there is no suggestion or motivation, either in Kettman, Ekins, or in the knowledge generally available to one of ordinary skill in the art, to combine the teachings of Kettman and Ekins as suggested in the Final Office Action. As a result, at least one of the three basic criteria for establishing a *prima facie* case of obviousness has not been met. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP 2142.

2. The basis for the obviousness rejection of the present claims is improper.

The Final Office Action states that "the rejection is based upon obviousness and Eikens et al. is relied upon to teach more than 64 sets in analyte analysis." (Final Office Action -- pages 4-5). However, Ekins does not teach "more than 64 sets" or any sets for that matter as the term "sets" is defined in the teachings of Kettman. For instance, Kettman teaches that sets are microsphere sets. In addition, the present claims recite "subsets of microspheres." Therefore, in the context of the present case, the term "set" refers to a set of microspheres.

Ekins, however, does not teach any microspheres at all. For instance, Ekins teaches different antibodies distributed over a single surface, each of which is specific to a different analyte being examined. Ekins teaches more than 64 different antibodies, each coupled to the same surface, but Ekins clearly does not teach "more than 64 sets in analyte analysis" as contended in the Final Office Action. Consequently, Ekins cannot be relied upon to teach more than 64 sets that can be used in analyte analysis. As such, this basis for the obviousness rejection of the present claims is improper.

3. The prior art appears to teach away from the combination of Kettman and Ekins suggested in the Final Office Action.

Even if the fluorescent markers of Ekins could be coupled to the surface of the microspheres of Kettman, the prior art appears to teach away from such a modification of the

microspheres of Kettman. In particular, Kettman appears to teach away from attaching fluorescent-based labels to a surface of the microspheres to distinguish the microspheres of one set from those of another. For instance, Kettman states that "Because the dyes are inside the microspheres, solvent conditions will not affect the dye characteristics." (Kettman -- page 241). Therefore, according to the teachings of Kettman, if the fluorescent-based labels are attached to a surface or a reagent on a surface of the microspheres (i.e., external to the microspheres), the solvent conditions will affect the dye characteristics of the microspheres thereby decreasing the uniformity of the fluorescence of microspheres in a set. In addition, as set forth in detail above, Kettman teaches that non-uniformity of fluorescence limits how many microsphere sets can be used in an assay. Therefore, Kettman teaches that attaching the fluorescent based labels of Ekins to the surface of the microspheres of Kettman will increase the non-uniformity of the fluorescent characteristics of the microspheres thereby reducing the number of microsphere sets that can be used in the assay. As such, the teachings of Kettman appear to teach away from the combination of Kettman and Ekins suggested in the Final Office Action. A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). MPEP 2141.02.

4. The prior art references must be considered in their entirety.

The Final Office Action states that "The arguments are not persuasive, as the instant claims have no limitations regarding 'how fluorescence is imparted'. Therefore, the markers being coupled or not is of no relevance to what is instantly claimed. Applicant is again reminded that Eikens et al. is relied upon solely to teach that more than 64 sets may be used in analyte analysis, with a reasonable expectation of success, as previously set forth." (Final Office Action -- page 5). However, as set forth in detail above, Ekins does not teach any "sets" that can be used in analyte analysis. Therefore, Ekins cannot teach or suggest that more than 64 sets can be used in analyte analysis with a reasonable expectation of success.

Regardless of how fluorescence is imparted to the presently claimed subsets of microspheres, the manner in which fluorescence is imparted to the assays in the prior art must be considered to determine if a reasonable expectation of success is taught or suggested by the prior art for "more than 64 sets," particularly since Kettman teaches that the 64 sets are distinguished by the fluorescence imparted to the microspheres. In addition, the prior art references must be considered in their entirety. A prior art reference must be considered in its entirety, i.e., as a whole. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). MPEP 2141.02. Therefore, portions of the prior art references cannot be arbitrarily selected to reject the present claims without considering what the combined teachings of the prior art as a whole suggest to one of ordinary skill in the art.

5. The prior art references, considered in their entirety, do not provide a reasonable expectation of success for combining the prior art as suggested in the Final Office Action.

Since Kettman teaches that "The vehicle for each separate measurement consists of a set of microspheres identifiable by characteristic fluorophores embedded in the particles" (Kettman -- page 234), the manner in which fluorescence is imparted to the particles is particularly relevant to the question of whether or not the prior art teaches or suggests a reasonable expectation of success for more than 64 sets that are identifiable by characteristic fluorophores embedded in the particles and can be used in analyte analysis. In particular, Kettman specifically teaches that the dyes used for discrimination of different microsphere sets are dissolved into the microspheres. In contrast, Ekins specifically teaches that the dyes used for discrimination of different analytes (e.g., antibodies) are attached directly to the analytes themselves and external to a substrate to which the analytes are attached. As such, Kettman and Ekins teach dramatically different technologies for fluorescent-based discrimination of analytes. In addition, as is known by one possessing the ordinary level of skill in the art at the time the invention was made, the technology for coupling fluorescent labels to antibodies cannot be used to dissolve fluorescent labels into a microsphere.

Since Ekins teaches that analyzing tens or hundreds of analytes is feasible using a technology different than the technology taught by Kettman, Ekins does not teach or suggest that using more than 64 microsphere sets for analyte analysis is technically feasible. In addition, Ekins does not disclose that fluorescent-based labels can be dissolved into microspheres. Simply put, Ekins does not teach or suggest any method for generating fluorescently-labeled probes other than attaching fluorescent-based labels to antibodies. Furthermore, Ekins does not teach or suggest that measuring tens or hundreds of analytes is technically feasible using the microsphere sets taught by Kettman. Moreover, since the teachings of Ekins do not even mention microspheres or microsphere sets, Ekins cannot teach or suggest that measuring tens or hundreds of analytes is technically feasible using microspheres or microsphere sets. As such, Ekins cannot teach or suggest a reasonable expectation of success for using more than 64 sets for analyzing analytes. Therefore, Ekins does not teach or suggest that more than 64 sets can be used in analyte analysis with any reasonable expectation of success as contended in the Final Office Action.

Even if the fluorescent markers of Ekins could be coupled to the surface of the microspheres of Kettman, Kettman does not teach or suggest a reasonable expectation of success for such modification of the microspheres of Kettman. In particular, the teachings of Kettman do not teach or suggest a reasonable expectation of success for attaching fluorescent-based labels to a surface of the microspheres to distinguish the microspheres of one set from those of another. For instance, Kettman states that "Because the dyes are inside the microspheres, solvent conditions will not affect the dye characteristics." (Kettman -- page 241). Therefore, according to the teachings of Kettman, if the fluorescent-based labels of Ekins are attached to a surface or a reagent on a surface of the microspheres (i.e., external to the microspheres), the solvent conditions will affect the dye characteristics of the microspheres thereby decreasing the uniformity of the fluorescence of microspheres in a set. In addition, Kettman teaches that non-uniformity of fluorescence limits how many microsphere sets can be used in an assay. Therefore, Kettman impliedly teaches that attaching the fluorescent based labels of Ekins to the surface of the microspheres of Kettman increases the non-uniformity of the fluorescent characteristics of the microspheres thereby reducing the number of microsphere sets that can be used in the assay. As such, Kettman does not teach or suggest a reasonable expectation of

success for applying the technology taught by Ekins to the microspheres of Kettman to produce more than 64 sets that can be used in analyte analysis.

For at least the reasons set forth above, even though Ekins discloses the ability of measuring "even hundreds" of substances in the same sample, there is no suggestion that the teachings of Kettman can be modified by the teachings Ekins to successfully enable measurements in a single sample using more than 64 sets of microspheres for more than 64 analytes disclosed by Kettman. Therefore, there is no suggestion in the prior art that the teachings of Kettman can be combined with the teachings of Ekins as suggested in the Final Office Action with any reasonable expectation of success for increasing the number of sets that can be used in the assay of Kettman and the number of analytes that can be measured in the assay of Kettman. Consequently, Kettman cannot be combined with Ekins to reject the present claims as *prima facie* obvious. To establish a *prima facie* case of obviousness, three basic criteria must be met…there must be a reasonable expectation of success…the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). MPEP 2142. The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). MPEP 2143.02.

Since the teachings of Kettman suggest that combining the teachings of Kettman and Ekins as suggested in the Final Office Action would reduce the uniformity of the microspheres in a set and the number of sets that can be used in a single mixture, the prior art impliedly contains a recognition that combining the teachings of the prior art produces a disadvantage or expected unbeneficial result. Therefore, the prior art does not contain a recognition, expressly or impliedly, that some advantage or expected beneficial result would have been produced by the combination of the prior art. The strongest rationale for combining references is a recognition, expressly or impliedly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent, that some advantage or expected beneficial result would have been produced by their combination. *In re Sernaker*, 702 F.2d 989, 994-5, 217 USPQ 1, 5-6 (Fed. Cir. 1983). MPEP 2144.

6. Since the teachings of the prior art conflict, the power of each reference to suggest solutions to one of ordinary skill in the art must be considered.

At the very least, the teachings of Kettman and Ekins conflict as to appropriate fluorescent labels that can be used to create probes for measurements of multiple substances in a single sample. In particular, the teachings of Kettman suggest to one of ordinary skill in the art that the fluorescent labels taught by Ekins are not suitable for multi-analyte measurements since, as set forth in detail above, Kettman teaches that solvent conditions may affect the dye characteristics of microspheres labeled with dyes that are external to the microsphere substrate. In addition, as set forth in detail above, Ekins clearly teaches that the fluorescent-based labels are attached to an antibody coupled to a surface of a substrate (i.e., the labels are external to the substrate). Therefore, the teachings of Kettman appear to discredit the teachings of Ekins. In any case, the teachings of the prior art certainly do not suggest to one of ordinary skill in the art the combination of Kettman and Ekins as suggested in the Final Office Action. The test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art, and all teachings in the prior art must be considered to the extent that they are in analogous arts. Where the teachings of two or more prior art references conflict, the examiner must weigh the power of each reference to suggest solutions to one of ordinary skill in the art, considering the degree to which one reference might accurately discredit another. *In re Young*, 927 F.2d 588, 18 USPQ2d 1089 (Fed. Cir. 1991). MPEP 2143.01.

7. The cited art does not suggest the desirability of the combination of the teachings of Kettman and Ekins.

For at least the reasons set forth above, the prior art does not suggest the desirability of combining the teachings of Kettman with the teachings of Ekins. Therefore, even if the teachings of Kettman and Ekins can be combined as suggested in the Final Office Action, the resulting combination is not obvious and is not sufficient to establish *prima facie* obviousness of the present claims. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). MPEP 2143.01.

8. Since there is no objective reason to combine the teachings of the references, even if the references teach that all aspects of the claimed invention were individually known in the art, the references are not sufficient to establish a *prima facie* case of obviousness.

Even if the references teach every element of the claims as contended by the Examiner, since there is simply no teaching, suggestion, or motivation to combine or modify the teachings of Kettman with the teachings of Ekins as suggested in the Final Office Action, a rejection based on a *prima facie* case of obviousness is improper. The combination of the references taught every element of the claimed invention, however without a motivation to combine, a rejection based on a *prima facie* case of obvious was held improper. MPEP 2143.01.

For at least the reasons set forth above, there is simply no objective reason to combine the teachings of the references as suggested in the Final Office Action. As such, even if modifying the teachings of Kettman with the teachings of Ekins as suggested in the Final Office Action would have been well within the ordinary skill of the art at the time the claimed invention was made, and if the references relied upon teach that all aspects of the claimed invention were individually known in the art, the combination of the prior art suggested in the Final Office Action is not sufficient to establish a *prima facie* case of obviousness. A statement that modifications of the prior art to meet the claimed invention would have been " 'well within the ordinary skill of the art at the time the claimed invention was made'" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). MPEP 2143.01.

9. The Examiner has failed to adequately support and/or establish a *prima facie* case of obviousness.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success.

Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations. MPEP § 2143. These three criteria have not been met by the Examiner in the present case. For example, there is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine Kettman and Ekins as suggested in the Final Office Action, as set forth in detail in the above Arguments. Second, as set forth in detail in the above Arguments, there is no reasonable expectation of success for combining Kettman and Ekins. Finally, Kettman and Ekins do not teach or suggest all claim limitations. Therefore, a *prima facie* case of obviousness has not been established.

* * *

As explained in the above Arguments, there is no teaching, suggestion, or motivation to modify or combine the cited art to teach the limitations of claims 1 and 7. For at least these reasons, claims 1 and 7 are patentably distinct over the cited art. In addition, dependent claims 2, 5-6, 40, and 41 are also patentably distinct over the cited art for at least the same reasons as their respective base claim. Therefore, the rejection of claims 1-2, 5-7, 40, and 41 under 35 U.S.C. 103 is asserted to be erroneous.

B. Claims 3-4

Because claims 3-4 are dependent from claim 1, the arguments presented above for patentability of claim 1 apply equally to claims 3-4, and are herein incorporated by reference. Claim 3 further recites that the claimed characteristic fluorescence signatures are derived from at least three fluorescent dyes incorporated in the microspheres. Claim 4 further recites that the claimed characteristic fluorescence signatures are derived from at least four fluorescent dyes incorporated in the microspheres. These additional recitations make claims 3-4 separately patentable over the cited art, as described in more detail below.

1. The cited art does not teach or suggest microspheres of one subset that are distinguishable from those of another subset by their characteristic fluorescence signatures derived from at least three fluorescent dyes incorporated into the microspheres.

Kettman states that "the dyes we used for classification are inside the microsphere." (Kettman -- page 241). Kettman also states that "Several observations have been made regarding the use of dyes dissolved in the microspheres…Additionally, as the dye content is increased, the spectrum of the combination of two dyes changes." (Kettman -- page 241). In addition, Kettman states that "The illumination of the FACScan (488 nm) is not optimal for the excitation of the two dyes used to emit Fl2 and Fl3." (Kettman -- page 239). Therefore, Kettman discloses microsphere subsets that are distinguishable from other microsphere subsets by characteristic fluorescence signatures that are derived from two fluorescent dyes incorporated into the microspheres. Ekins does not disclose microspheres. As such, neither Kettman nor Ekins teaches microspheres of one subset that are distinguishable from those of another subset by their characteristic fluorescence signatures derived from at least three fluorescent dyes incorporated into the microspheres, as recited in claims 3-4. In addition, Kettman and Ekins provide no suggestion or reasonable expectation of success that microspheres of one subset can be distinguishable from those of another subset by characteristic fluorescence signatures derived from at least three fluorescent dyes incorporated into the microspheres. Consequently, Kettman and Ekins cannot be modified or combined to reject claims 3-4 as *prima facie* obvious. As such, the Examiner has failed to establish a *prima facie* case of obviousness of claims 3-4, and rejection of claims 3-4 under 35 U.S.C. § 103 is asserted to be erroneous.

* * *

For the foregoing reasons, it is submitted that the Examiner's rejection of claims 1-7, 40, and 41 was erroneous, and reversal of the Examiner's decision is respectfully requested.

The Commissioner is hereby authorized to charge the required fee(s) to deposit account number 50-3268/5868-02801.

Respectfully submitted,
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Date: January 8, 2007

VIII. CLAIMS APPENDIX

The present claims on appeal are as follows.

1. A Multi-Analyte Profile (MAP) Test Panel comprising 75 or more subsets of microspheres, wherein the microspheres of one subset are distinguishable from those of another subset by their characteristic fluorescence signatures, and wherein the microspheres of the one subset are coupled to at least one reagent designed to interact selectively with a predetermined analyte.

2. The MAP Test Panel of claim 1, further comprising 100 or more subsets of microspheres.

3. The MAP Test Panel of claim 1, wherein the characteristic fluorescence signatures are derived from at least three fluorescent dyes incorporated in the microspheres.

4. The MAP Test Panel of claim 1, wherein the characteristic fluorescence signatures are derived from at least four fluorescent dyes incorporated in the microspheres.

5. The MAP Test Panel of claim 1, wherein the at least one reagent comprises a small molecule, natural product, synthetic polymer, peptide, polypeptide, polysaccharide, lipid, nucleic acid, or combinations thereof.

6. The MAP Test Panel of claim 1, wherein the predetermined analyte comprises a drug, hormone, antigen, antibody, protein, enzyme, DNA, RNA, or combinations thereof.

7. A kit for assaying 75 or more predetermined analytes in a single pass through a flow analyzer comprising a Multi-Analyte Profile (MAP) Test Panel comprising 75 or more subsets of microspheres, wherein the microspheres of one subset are distinguishable from those of another subset by their characteristic fluorescence signatures, wherein the microspheres of the one subset are coupled to at least one reagent designed to interact selectively with a predetermined analyte, and wherein the kit further comprises vials, supplemental reagents, or any combination thereof.

39. (withdrawn) A method of using a Multi-Analyte Profile (MAP) Test Panel to assess a subject's health or medical condition comprising:

(a) exposing the one or more test samples obtained from a subject to a Multi-Analyte Profile (MAP) Test Panel comprising 20 or more subsets of microspheres, the microspheres of one subset being distinguishable from those of another subset by their characteristic fluorescence signatures and harboring at least one reagent designed to interact selectively, if not specifically, with a predetermined analyte, which interaction generates biochemical data concerning the predetermined analyte;

(b) gathering the biochemical data, if any, generated from the exposure;

(c) comparing the biochemical data generated from the one or more samples obtained from the subject with accumulated biochemical data generated from test samples taken periodically from at least about 1,000 individuals over a given time interval, which accumulated biochemical data provide a relationship between one or more predetermined analytes and the health or medical condition of a plurality of individuals whose accumulated biochemical data share similar features; and

(d) assessing the health or medical condition of the subject based, at least in part, on the results of the comparison.

40. The MAP Test Panel of claim 1, further comprising 200 or more subsets of microspheres.

41. The MAP Test Panel of claim 1, further comprising 300 or more subsets of microspheres.

IX. EVIDENCE APPENDIX

none

X. RELATED PROCEEDINGS APPENDIX

none